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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MCDONNELL BOEHNEN HULBERT @ BERGHOFF LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,588	FRANCIS-LANG ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *4,5,7-15 and 18-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,16 and 17* is/are rejected.

7)☒ Claim(s) *1-3,6,16 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0306*1106.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of Invention I, Claims 2, 3, 6, 16, and 17, in their response of April 27, 2007 is acknowledged. The elected invention is directed to a method for identifying a modulator using a cellular proliferation assay system comprising a casein kinase. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-25 are pending. Claims 4, 5, 7-15, and 18-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-3, 6, 16, and 17 are hereby examined.

Priority

The priority date granted for the instant invention is August 7, 2002, the filing date of US60/401,739, which disclosed the elected invention.

Oath-Objections

The Oath is objected to because the change of address for Haiguang Zhang in the Oath/Declaration received February 4, 2005 is not initialed or dated. See M.P.E.P. 605.04(a), which states that, any changes made to the Oath/Declaration should be initialed and dated by the Applicants prior to execution. The Office will not consider whether noninitialed and/or nondated alterations were made before or after signing of the Oath or Declaration but will require a new Oath or Declaration (37 CFR 1.64).

Information Disclosure Statement

Parts of the Information Disclosure Statement filed March 24, 2005 fail to comply with 37 CFR 1.98(a)(1). Citations 1-16 fail to provide a date. The information disclosure statement

has been placed in the application file, but the information referred to in citations 1-16 has not been considered. If Applicants wish for said references to be considered, a supplemental, corrected Information Disclosure Statement should be submitted. Any subsequent rejection, based on consideration of the supplemental Information Disclosure Statement, will not be considered a new grounds for rejection.

Specification-Objections

The specification is objected to for containing hyperlinks. USPTO policy does not permit the USPTO, i.e, via an issued patent, to link to any commercial sites, since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. Hyperlinks and other forms of browser-executable code, especially commercial site URLs, are not to be included in a patent application. (MPEP 608.01) The specification should be carefully checked and all URLs and reference to any web site removed.

Claims-Objections

Claims 1-3, 6, 16, and 17 are objected to for reciting non-elected subject matter.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-3, 6, 16, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reason.

For Claims 1 and 16, the phrase "agent-biased activity" renders the claims indefinite. The skilled artisan would not know the meets and bounds of the recited invention. Claims 2, 3,

6, and 17, as dependent from Claim 1 and/or Claim 16, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the same reasons.

For Claims 1, line 5, and Claim 16, line 6, the phrase "the system" lacks antecedent basis and, thus, renders the claims indefinite. Claims 2, 3, 6, and 17, as dependent from Claim 1 and/or Claim 16, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the same reasons. Said phrase should be corrected to "the assay system".

For Claim 16, the phrase "a secondary assay system" renders the claims indefinite. It is unclear whether said second assay system (i) must consist of the same steps used the first assay system, (ii) must consist of different steps from those used in the first assay system, or (iii) may consist of the same or different steps from those used in the first assay system. Claim 17, as dependent from Claim 16, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the same reasons. For purposes of examination, it is assumed that said secondary assay system may consist of the same or different steps from those used in the first assay system.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-3, 6, 16, and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the effect of reducing expression of the proteins set forth by SEQ ID NO: 1, 8, and 11 on cell proliferation, does not reasonably provide enablement for a method of identifying a p21-pathway modulator by testing the effect of

any compound in any assay system comprising any CSNK1G. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claim 1 is so broad as to encompass a method of identifying a p21-pathway modulator by testing the effect of any compound in any assay system comprising any CSNK1G. Claims 2, 3, 6, 16, and 17 are so broad as to encompass a method of identifying a p21-pathway modulator by testing the effect of any compound in any cellular assay system comprising any CSNK1G. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methods broadly encompassed by the claims.

The specific reagents and steps used for any method determine the method's success. Predictability of which steps and reagents can be used to obtain the desired identification of p21-

pathway modulators requires a knowledge of, and guidance with regard to how said steps and reagents relate to the desired objective. Which of the essentially infinite number of assay systems that can be used to accomplish the desired goal has not been taught. In addition, predictability of how any successful method can be altered requires a knowledge of, and guidance with regard to how the steps and regents of the method affect the desired identification of p21-pathway modulators. However, in this case the disclosure is limited to a method of determining the effect of reducing expression of the proteins set forth by SEQ ID NO: 1, 8, and 11 on cell proliferation.

While many assay methods are known, it is not routine in the art to screen essentially any assay for being useful to identify a p21-pathway modulator by testing the effect of any compound in any said assay system comprising any CSNK1G. Furthermore, the steps and reagents to be used with a reasonable expectation of success in obtaining the desired identification of a p21-pathway modulator using any comprising any CSNK1G are limited and unpredictable. In addition, one skilled in the art would expect any tolerance to modification of a successful method to diminish with each further and additional modification of steps and reagents used.

The specification does not support the broad scope of Claim 1, which encompasses any method of identifying a p21-pathway modulator by testing the effect of any compound in any assay system comprising any CSNK1G. The specification does not support the broad scope of Claims 2, 3, 6, 16, and 17, which encompasses any method of identifying a p21-pathway modulator by testing the effect of any compound in any cellular assay system comprising any CSNK1G. The specification does not support the broad scope of Claims 1-3, 6, 16, and 17

because the specification does not establish: (A) the structure and function of any CSNK1G to be used in the recited method; (B) regions of the protein structure which may be modified without affecting the desired activity; (C) the general tolerance of the desired activity to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; (E) the steps and regents to be successfully used to identify p21-pathway modulators; (F) how any steps and regents may be modified without affecting the desired goal of the method; (G) the general tolerance of the steps and regents to modification and extent of such tolerance; (H) a rational and predictable scheme for modifying any steps and regents with an expectation of obtaining the desired identification of p21-pathway modulators; and (I) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for identifying a p21-pathway modulator by testing the effect of any compound in any assay system, or any cellular assay system, comprising any CSNK1G. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-3, 6, 16, and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1-3, 6, 16, and 17 are directed to a genus of methods for identifying a p21-pathway modulator by testing the effect of any compound in any assay system, or any cellular assay system, comprising any CSNK1G. The specification teaches no such methods. Given this lack of description of representative species encompassed by the genera of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Beyaert et al, 1995. Beyaert et al teach that CKI-7 [N-(2-aminoethyl)-5-chloroisoquinolin 8-sulphonamide) is a cell-permeable inhibitor of casein kinase I (pg 23296, parg 3). Beyaert et al further teach a cellular assay system comprising casein kinase I, wherein CKI-7 is used to demonstrate that inhibition of casein kinase I reduces the phosphorylation and activity of the p75TNF receptor and

enhances apoptosis (Fig 3, 4, and Table II). Therefore, Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Beyaert et al, 1995.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 6, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beyaert et al, 1995 in view of Gehr et al, 1992. The teachings of Beyaert et al are described above. Beyaert et al do not teach a method for testing the effect of the CKI-7 casein kinase I inhibitor on cellular proliferation in a secondary assay system. Gehr et al teach that the p75TNF receptor mediates proliferation in peripheral blood mononuclear cells (PBMCs) (Figs 5 & 7). It would have been obvious to a person of ordinary skill in the art to test the effect of the cell-permeable CKI-7 casein kinase I inhibitor of Beyaert et al in the PBMC proliferation assay of Gehr et al. Motivation to do so derived from the desire to determine if casein kinase I modulates the effect of the p75TNF receptor on proliferation. The expectation of success is high, as Beyaert et al teach methods for treating intact cells with CKI-7, while Gehr et al teach methods for detecting proliferation in PBMCs. Therefore, Claims 1, 2, 6, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beyaert et al, 1995 in view of Gehr et al, 1992.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshii et al, 2002 in view of Beyaert et al, 1995. Yoshii et al teach that phosphorylation of galectin-3 by casein kinase I causes up-regulation of $p21^{WAF1/CIP1}$, as measured by Western blotting (Fig 4).

Yoshii et al do not teach using their Western blotting method to identify agents that inhibit galectin-3 phosphorylation by casein kinase I and, thereby, inhibit $p21^{WAF1/CIP1}$ expression. It would have been obvious to a person of ordinary skill in the art to test the effect of the cell-permeable CKI-7 casein kinase I inhibitor of Beyaert et al in the method of Yoshii et al. Motivation to do so derives from the desire to pharmacologically confirm that phosphorylation of galectin-3 by casein kinase I causes up-regulation of $p21^{WAF1/CIP1}$. The expectation of success is high, as Beyaert et al teach methods for treating intact cells with CKI-7, while Yoshii et al teach methods for detecting galectin-3 phosphorylation and $p21^{WAF1/CIP1}$ up-regulation. Therefore, Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshii et al, 2002 in view of Beyaert et al, 1995.

Claims 1, 2, 3, 6, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshii et al, 2002 in view of Beyaert et al, 1995 and further in view of Timchenko et al, 1996. The teachings of Yoshii et al and Beyaert et al are described above. Neither Yoshii et al, Beyaert et al, nor the combination thereof teach a method for testing the effect of the CKI-7 casein kinase I inhibitor on cellular proliferation in a secondary assay system. Timchenko et al teach a method to demonstrate that $p21^{WAF1/CIP1}$ inhibits proliferation; fibrosarcoma cells having defective p21 function have reduced proliferation (Fig 8). It would have been obvious to a person of ordinary skill in the art to use fibrosarcoma cells to test the effect of the CKI-7 casein kinase I inhibitor of Beyaert et al in the galectin-3 phosphorylation assay of Beyaert et al as well as the proliferation assay of Timchenko et al. Motivation to do so derives from the desire to test whether the phosphorylation of galectin-3 by casein kinase I, and subsequent up-regulation of $p21^{WAF1/CIP1}$, inhibits proliferation in fibrosarcoma cells. The expectation of success is high as

Beyaert et al teach methods for treating intact cells with CKI-7, Beyaert et al teach that phosphorylation of galectin-3 by casein kinase I causes up-regulation of $p21^{WAF1/CIP1}$, and Timchenko et al teach methods for testing the role of $p21^{WAF1/CIP1}$ in the proliferation of fibrosarcoma cells. Therefore, Claims 1, 2, 3, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshii et al, 2002 in view of Beyaert et al, 1995 and further in view of Timchenko et al, 1996.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.
Art Unit 1652

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER